

IV. REMARKS

Applicant has reviewed the final Office Action mailed March 10, 2005 ("Office Action").

A. Invention

The present invention is generally directed to systems which use phycobilisomes or their equivalents for receiving and transferring light energy.

B. Amendments

Claims 53 and 61 have been amended. As amended, claim 61 recites a "conversion means" which should be interpreted under §112 ¶6 to include the corresponding structures disclosed in the specification and their equivalents.

Claims 71-74 have been withdrawn by the Examiner as being directed to a non-elected invention.

At the request of the Examiner, claims 1, 11, 15, 22, 31, 43-49, 55, and 71-74 are cancelled as being withdrawn claims directed to non-elected subject matter. Claim 54 is additionally cancelled.

Claims 75-87 have been added.

Claims 50-53, 59-70, and 75-87 are currently pending.

C. Interview

In an interview conducted October 21, 2005, Applicant's representatives and the Examiner discussed the claims, the prior art applied in the pending claim rejections, and the scope of the claims under §112 ¶6. The Examiner agreed that the "conversion means" recitation in the claims is limited to the embodiments disclosed in Applicant's specification

and equivalents thereof. The Applicant's representative stated that the recitation "conversion means" (as recited in independent claims 50 and 61) refers to three distinct phycobilisome embodiments disclosed in the specification (and equivalents thereof). Applicant notes that those three embodiments relate to: (1) an isolated, soluble, stabilized phycobilisome; (2) a phycobilisome conjugated to a molecular species selected from the group consisting of ligands, receptors, and signal-generating molecules; and (3) a phycobilisome immobilized on a manufactured solid support.

The Examiner requested that Applicant show that the phycobilisome "conversion means" embodiments disclosed in the specification do not correspond to the phycobilisome structures disclosed in U.S. Patent No. 4,857,474 to Waterbury et al. (the "Waterbury patent"). More specifically, the Examiner requested Applicant to provide evidence to rebut the Examiner's presumption that Waterbury's phycobilisomes are "stabilized" within Applicant's definition of that term. Applicant submits herewith a Declaration under 37 C.F.R. §1.132 that demonstrates why Applicant's stabilized phycobilisomes distinguish over Waterbury and other prior art.

D. Declaration under 37 C.F.R. §1.132

Applicant hereby submits a Declaration under 37 C.F.R. §1.132 in response to the Examiner's request for evidence showing that Applicant's disclosed "conversion means" embodiments (specifically, the stabilized phycobilisome embodiment) distinguish over the prior art. The Yamanaka article, which discloses the phycobilisome preparation method used in the Waterbury patent, is enclosed as an Exhibit to the Declaration.

As explained in more detail in the Declaration, Applicant's stabilized phycobilisomes (a disclosed "conversion means" embodiment) are "stabilized," while the phycobilisome preparations of the Yamanaka article and the Waterbury patent are *not* stabilized. Phycobilisomes, by themselves, will not function as a "conversion means" unless they are stabilized. Without stabilization, they fall apart as documented in the Yamanaka article, e.g., in Figures 5A-5D. While Applicant achieves the recited "directional transfer" of energy as demonstrated by an extensive shift in wavelength fluorescence (discussed in the Specification), this result is not reliably or reproducibly obtained in the prior art because of the tendency of the phycobilisome structure to dissociate when using prior art methods of preparation.

E. Objection to Drawings

The Office has objected to the Drawings under 37 CFR 1.83(b) and has requested corrected drawing sheets in compliance with 37 CFR 1.121(d) to avoid abandonment of the application. In particular, the Office notes that the current Drawings fail to show the structural elements of the recited claims.

Accordingly, Applicant submits herewith new Drawings that show the structural elements as recited in the claims. The new Drawings are supported by the application and claims as originally filed, and no new matter has been added.

F. Objection to claims 54, 61, and 62

The Office objected to claim 62 under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

The Office objected to claims 61 and 54 under 37 C.F.R. §1.75 as being a substantial duplicate of claims 62 and 68, respectively. As stated in the Office Action, it is proper after allowing one claim to object to another as being a substantial duplicate of the allowed claim. At present, none of the claims (including claims 62 and 68) have been allowed, so the instant objection is premature. Applicant notes that this issue may be revisited if and when any of these allegedly identical claims are allowed. However, in regard to the instant objection, Applicant states the following.

Claim 62 recites “[t]he system of claim 61, wherein said processing means comprises a phycobilisome.” Claim 61 does not specifically recite a “phycobilisome.” In a very straightforward fashion, claim 62 limits the scope of claim 61 by requiring that the “processing means” (which “receiv[es] and process[es] said light energy”) comprise a phycobilisome. Claim 62 accordingly has a different scope than claim 61 because it recites a phycobilisome as a “processing means.” The scope of claim 61 is more broad than that of claim 62. For example, claim 61 covers embodiments wherein the processing means comprises an optical fiber (and not a phycobilisome).

Applicant further notes that in various exemplary embodiments disclosed in the specification, the “conversion means” may comprise a phycobilisome. In Claim 62, the “processing means,” a structural element physically distinct from the “conversion means,” comprises a phycobilisome. Claim 62 may accordingly cover embodiments with (at least) two phycobilisomes that accomplish two different functions.

Claims 54 and 68 also have a different scope. In claim 54, the conversion means directionally transfers light energy, and the processing means receives and transfers the

directionally transferred light energy. In contrast, claim 68 does not recite that the structural components directionally transfer light energy or receive and transfer directionally transferred light energy.

Regardless, claim 54 has been cancelled, rendering the objection to claim 54 moot.

Accordingly, Applicant respectfully requests that the instant objections to claims 54, 61, and 62 be withdrawn.

G. Rejection of Claim 67 under 35 U.S.C. §112, second paragraph

Claim 67 was rejected under 35 U.S.C. §112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Office Action asserts that “claim 67 fails to set forth any details beyond that already recited in claim 61.” Office Action, page 4.

Claim 67 recites “[a]n environmentally responsive sensor comprising the system of claim 61.” Applicant notes that claim 61 must be sufficiently definite as it is not the subject of an indefiniteness rejection.

However, even if the Office’s assertion that claim 67 does not set forth additional details beyond that recited in claim 61 were true, the failure to specify additional details beyond claim 61 would not make the claim “indefinite.” As stated in MPEP §703.03(d), the instant rejection is not appropriate “[i]f the scope of the claimed subject matter can be determined by one of ordinary skill in the art.” In other words, if one of ordinary skill in the art can understand the metes and bounds of the claim, then the claim is not indefinite. The claim simply recites the system of claim 61 (which is adequately definite) comprised

in a sensor that responds to its environment. The subject matter of this claim can be determined by one of ordinary skill in the art. Hence, this claim is not indefinite.

Accordingly, Applicant respectfully requests that the instant rejection of claim 67 be withdrawn.

H. Rejection of Claims 50-53, 59, and 60 under 35 U.S.C. §102(b) as being anticipated by Kane

Claims 50-53, 59, and 60 were rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,037,615 to Kane (“Kane”). During the Interview the Examiner indicated that, because any equivalent to the recited “conversion means” must provide directional energy transfer, the instant rejection over Kane is improper.

Accordingly, Applicant respectfully requests that the instant rejection be withdrawn. Applicant also submits the following additional arguments.

As noted in Applicant’s prior response, the Office Action alleges that in accordance with the specification the “conversion means” recited in independent claim 50 operates to excite a first fluorophore, which excitation emission effects excitation of a second acceptor fluorophore. Office Action, page 5. Since the tethered energy transfer pair of fluorophores in Kane operates in this manner, the indicator composition of Kane is urged to fully anticipate the claimed conversion means. *Id.* Applicant respectfully disagrees and traverses this rejection on the following grounds.

For convenience, original claim 50 is repeated as follows.

50. A system for processing a light signal comprising:
conversion means for receiving ultraviolet or visible light and directionally transferring light energy of said light and
processing means for receiving and processing said directionally transferred light energy.

When an element is claimed using language falling under the scope of 35 U.S.C. § 112, 6th paragraph (often broadly referred to as means- or step-plus-function language), the specification must be consulted to determine the structure, material, or acts corresponding to the function recited in the claim. M.P.E.P. § 2111.01 (citing *In re Donaldson*, 16 F.3d 1189, 29 USPQ2d 1845 (Fed. Cir. 1994)). The application of a prior art reference to a means- (or step-) plus-function limitation requires that the prior art element perform the identical function specified in the claim. M.P.E.P. § 2182. However, if a prior art reference teaches identity of function to that specified in a claim, then under *Donaldson* an examiner carries the initial burden of proof for showing that the prior art structure or step is the same as or equivalent to the structure, material or acts described in the specification, which has been identified as corresponding to the claimed means- (or step-) plus-function. *Id.* (emphasis in original). In order to make a *prima facie* case of equivalence, the examiner must show that the prior art element (i) performs the function specified in the claim, (ii) is not excluded by any explicit definition provided in the specification for an equivalent, and (iii) is an equivalent of the means- (or step-) plus-function limitation. See M.P.E.P. § 2183. One factor that will support a conclusion that the prior art element is an equivalent is: the prior art element is a structural equivalent of the corresponding element disclosed in the specification. *Id.* (citing *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990)). That is, the prior art element performs the function specified in the claim in substantially the same manner as the function is performed by the corresponding element described in the specification. *Id.* (emphasis added).

The Examiner's assertion that the recited conversion means operates in the same manner as, and hence is a structural equivalent of, the tethered energy transfer pair of fluorophores in Kane is unsoundly based. Under §112 ¶ 6, the "conversion means" refers to the structure(s) recited in the specification and their equivalents. Applicant's specification explicitly discloses various embodiments comprising a phycobilisome for use as a conversion means. A phycobilisome is defined as a supramolecular light-absorbing structure comprising at least one phycobiliprotein-containing rod. Applicant's Specification, page 8, lines 22-23. Phycobilisomes contain two or more phycobiliproteins specifically connected by one or more linker polypeptides, where the two or more phycobiliproteins are in a particular orientation dictated by the linker polypeptide, with the orientation typically facilitating energy transfer between the phycobiliproteins. *Id.* at page 8, line 28 to page 9, line 2. Kane is directed toward a fluorescence energy transfer indicator that includes a membrane or plug 19 having a tethered pair fluorescence energy transfer indicator comprising a fluorescent energy donor and a colorimetric indicator acceptor. *See* Kane, abstract and col. 5, 11. 47-58. Kane teaches using a small molecule fluorescent dye as the fluorescent energy donor. *See* *Id.* at column 4, lines 44-66. No teaching is provided with respect to the use of supramolecular structures such as phycobilisomes. Clearly, Kane's fluorescent dye has a substantially different structure than that of a phycobilisome, *i.e.*, a supramolecular light-absorbing structure comprising at least one phycobiliprotein-containing rod.

Applicant notes that Kane's tethered pair fluorescence energy transfer indicator does not directionally transfer light energy in substantially the same way as a

phycobilisome. Directional energy transfer within phycobilisomes occurs from one or more “sensitizing species” to a terminal acceptor. Applicant’s Specification, page 7, line 23-24 (emphasis added). The light-harvesting properties of phycobilisomes depend on an intrinsic structural and functional “sidedness,” meaning that photons are collected from one “side” (i.e., peripheral rod(s)) and re-emitted from a second “side” (i.e., the terminal acceptor). *Id.* at page 49, lines 23-29. This distinct and useful property is absent in Kane. For example, Kane’s fluorescent dye *per se* lacks any type of intrinsic directional energy transfer property, as it is well understood that a dye fluorophore can emit a photon in any direction spontaneously.

Claims 51-53, 59, and 60 are not anticipated by Kane at least because they depend from independent claim 50.

Response to Arguments

In the present Office Action, the Office rejected Applicant’s prior arguments that Kane does not disclose Applicant’s preferred embodiment (i.e., the phycobilisome embodiment) because claims under §112 ¶6 are not construed to be limited by preferred embodiments. While it is true that such claims are not necessarily limited by preferred embodiments, claims under §112 ¶6 are limited to embodiments actually disclosed in the specification (and their equivalents). If the preferred phycobilisome embodiment is the only disclosed embodiment, then the claims must be limited to this embodiment (and its equivalents).

Applicant continues to submit that Kane does not disclose or suggest the recitations of claims 50-53, 59, and 60 as interpreted under §112 ¶ 6. Applicant has explained in

detail why Kane fails to disclose or suggest the phycobilisome embodiment. To the extent that Examiner believes that Kane (or another reference) anticipates or suggests an embodiment in Applicant's specification (or equivalent) *other than* phycobilisomes, then it is the Examiner's burden to identify such embodiment and show how such embodiment (or equivalent) is disclosed. As it stands, however, the Examiner has not identified any embodiment of the present invention other than phycobilisomes that may be disclosed or suggested by the prior art. Kane and its tethered pair fluorescence energy transfer indicator do not correspond to any embodiments in Applicant's specification (or their equivalents).

Further, the Office's reliance on the doctrine of claim differentiation to support the argument that the claims are not limited to phycobilisomes in light of claim 54 is moot because claim 54 has been cancelled.

Accordingly, Applicant respectfully requests that the instant rejection be withdrawn.

I. Rejection of Claims 54 and 61-70 under 35 U.S.C. §103(a) as being unpatentable over Waterbury in view of Hendrix

Claims 54 and 61-70 were rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 4,857,474 to Waterbury et al. ("Waterbury") in view of U.S. Patent No. 4,707,454 to Hendrix ("Hendrix"). Claim 54 has been cancelled. Claim 61 has been amended to remove the recitation "~~wherein said conversion means includes a structure comprising a phycobilisome.~~" Accordingly, claim 61 as amended has a scope governed by §112 ¶6, as described above.

Applicant submits that the instant rejection is improper for the reasons demonstrated in the Declaration submitted herewith, which rebuts the Examiner's

presumption that Waterbury's phycobilisomes are "stabilized" as defined and supported in Applicant's specification. The Declaration shows that the Waterbury phycobilisomes (and the Yamanaka phycobilisome preparations to which Waterbury refers) are not stabilized. Because they are not stabilized, they dissociate and lose their desirable light-transmitting properties. Accordingly, Applicant respectfully requests that the instant rejection be withdrawn. Applicant also submits the following additional arguments.

Independent claim 61 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 4,857,474 to Waterbury *et al.* ("Waterbury") in view of U.S. Patent No. 4,707,454 to Hendrix. Office Action at page 6. Particularly, the Office Action asserts that Waterbury teaches or suggests all the limitations of claim 54 except for the particular optical structure utilized to produce the emission spectra of phycobilisomes. *Id.* In an attempt to cure such a deficiency, Hendrix is introduced as disclosing an apparatus suited to illuminating and monitoring fluorescent emissions for phycobiliproteins, which includes a light source and detector communicating with the fluorescing material via optical fibers. *Id.* at page 5. Applicant respectfully disagrees and traverses this rejection on the following grounds.

Waterbury, either taken alone or in combination with Hendrix, fails to teach or suggest a "conversion means" as recited in amended claim 61 and as interpreted under §112 ¶6. Waterbury provides a group of phycobiliproteins, *i.e.*, the constituents of phycobilisomes, useful as fluorescent moieties in conjugates. Waterbury, col. 4, ll. 33-37 and Example 1 at col. 7, line 45 to col. 10, line 62. Hendrix teaches fluorescent chlorophyll-labeled assay reagents. *See* Hendrix, abstract.

Under §112 ¶6, the “conversion means” refers to the structure(s) recited in the specification and their equivalents. Although Waterbury discloses measuring an emission spectra of a phycobilisome, neither Waterbury nor Hendrix discloses or suggests the structures recited in Applicant’s specification (or their equivalents), which include, for example: (a) an isolated, soluble, stabilized phycobilisome; (b) a phycobilisome conjugated to a molecular species selected from the group consisting of ligands, receptors, and signal-generating molecules; and (c) a phycobilisome immobilized on a manufactured solid support.

Thus, neither reference discloses or suggests a “conversion means” (under §112 ¶6) for receiving ultraviolet or visible light and directionally transferring light energy of said light as disclosed in Applicant’s specification (or an equivalent of the embodiments disclosed in Applicant’s specification).

Response to Arguments

The Office asserts that “Applicant’s [prior argument that Waterbury teaches] measurement of phycobiliproteins rather than phycobilisomes” is incorrect in light of Waterbury’s disclosure, which states:

The absorption and fluorescence emission spectra of WH8103 physobilisomes [sic] are shown in FIG. 2. The emission spectrum is similar to the spectra observed for cyanobacterial phycobilisomes of various biliprotein compositions. Energy absorbed by the PUB chromophores of WH8103 phycoerythrin is transferred efficiently to the terminal energy acceptors of the phycobilisome, which are responsible for the 676-nm emission peak. The small emission peak at 563 nm represents the direct emission of fluorescence from phycoerythrin.

Waterbury, column 8, lines 48-58 (emphasis added). The phycobilisomes mentioned in this passage are used only to passively measure their emission spectra. As noted in

Waterbury, the “[p]hycobilisomes were prepared as described by Yamanaka et al. (*J. Biol. Chem.* 253: 8303 (1978),” which is a conventional preparation. Conventional measuring of emission spectra, by itself, does not teach or suggest any of the corresponding “conversion means” disclosed in Applicant’s specification (or any equivalents).

It should be noted that although Waterbury discloses the conventional measurement of phycobilisomes, the detailed disclosure of Waterbury does not refer to intact phycobilisomes, but rather to isolated components of phycobilisomes. The passage of Waterbury cited above is provided in reference to the description of Example 1, which “describes the evaluation and characterization of a phycoerythrin derived from a strain of *Synechococcus*...strain WH8103.” Col. 7, lines 46-49 (emphasis added). In the passage describing Example 1, Waterbury describes in detail how the phycoerythrin is separated and derived from the phycobilisome. Among other things, the phycobilisomes were dialyzed, run through ultracentrifugation, and the phycoerythrin zone was recovered by precipitation with ammonium sulfate. Thus, the only components that were isolated and functionally used in the Waterbury system were phycoerythrins, not phycobilisomes. Accordingly, Waterbury does not teach use of intact phycobilisomes. Hendrix does not remedy this deficiency.

The above arguments also apply to claims 62-70, which depend from independent claim 61.

For at least these reasons, Applicants respectfully request that the instant rejection be withdrawn.

V. CONCLUSION

For all the reasons set forth above, it is respectfully submitted that all outstanding rejections have been overcome or rendered moot. Further, all pending claims are patentably distinguishable over the prior art of record. All amendments are supported by the specification and claims as originally filed. Applicants accordingly submit that these claims are in a condition for allowance. Reconsideration and allowance of all claims are respectfully requested.

Authorization is hereby granted to charge or credit the undersigned's Deposit Account No. 50-0206 for any fees or overpayments related to the entry of this Amendment, including any extension of time fees and new claims fees.

Respectfully submitted,

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